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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/733,773	12/08/2000	Joseph P. Noel	SALK2410	2948

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EXAMINER

CLOW, LORI A

ART UNIT	PAPER NUMBER
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1631

13

DATE MAILED: 07/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/733,773

Applicant(s)

NOEL ET AL.

Examiner

Lori A. Clow, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) 17-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-16 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☒ Claim(s) 1-28 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 12.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. § 121:

- I. Claims 1-16, drawn to a method of identifying a binding agent based upon atomic modeling, classified in Class 702, subclass 27.
- II. Claims 17-18, drawn to a computer program for defining an interaction site, classified in Class 702, subclass 22.
- III. Claims 19-28, drawn to an isolated crystalline WW domain, classifies in Class 702, subclass 27.

The inventions are patentably distinct, each from the other, because:

The inventions of Group I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case, the method of Group I does not require the program of Group II.

The inventions of Group II and Group III are distinct in that they are unrelated. The computer program of Group II and the crystal of Group III are separate entities, one being chemical in nature and the other comprising software for manipulation of atomic data.

The inventions of Group I and Group III are distinct in that they are drawn to separate chemical entities. One is a method for identifying a binding agent which is a different chemical entity from the actual crystal structure of Group III.

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As such, the search for each method or product would not be co-extensive in scope and would pose undue search burden on the examiner if not restricted.

During a telephone conversation with Stephen Reiter on 6 June 2003 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-16. Affirmation of this election must be made by applicant in replying to this Office action. Claims 17-28 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Information Disclosure Statement

The IDS, filed 7 February 2003 has been entered and considered. An initialed copy of the form PTO-1449 is included with this office action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

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2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Raganathan et al. (Cell (1997) Vol.89, pages 875-886; PTO 1449 Reference A24) in view of Verdecia et al. (Nature Structural Biology (2000) August, Vol. 7, No.8, pages 639-643) in further view of Lu et al. (US 6,495,376).

Raganathan et al. do disclose both structural and functional analyses of Pin1, which is a WW domain containing protein (see abstract). They describe in depth the overall architecture and domain topology of Pin1, which consists of two structural domains organized around a hydrophobic cavity (page 876, column 2-page 877, column 1), the surface structure properties (page 877, column 2-page 878), the substrate specificity (page 880, column 1-2), and the reaction mechanism (page 880, bottom column 2-page 883, column 2). Also disclosed are computer generated (MOLSCRIPT, Raster3D and RIBBONS software) ribbon models of Pin1 detailing the PPIase domain and the interdomian cavity (see Figure 1, A and B). Raganathan et al. do not

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disclose the contacting said potential binding agents in the presence of a WW domain substrate with the WW domain in order to determine binding preference (competition).

However, Verdicia et al. disclose the structural basis for phosphoserine-proline recognition by group IV WW domains. In particular, they define an interaction site by measuring the affinity of full-length Pin1 and its isolated PPIase and WW domains for peptides labeled at their N-termini with rhodamine using fluorescence anisotropy (page 640, column 1, lines 1-3). With this information X-ray crystallography was carried out for the Pin1-phosphopeptide complex and atomic coordinates identified, such that specific binding domains were elucidated (phosphopeptide=Tyr-P.Ser-Pro-Thr-P.Ser-Pro-Ser), meeting the limitations of claim 1-2, 6, 7, 8, 10-16. Verdicia et al. do not disclose the use of inhibitory, antagonistic, or agonistic agents.

However, Lu et al. teach methods and compositions of WW-domains as phosphoserine and phosphothreonine binding modules. The invention relates to methods of modulating protein-protein interactions comprising modulating the binding of WW-domain polypeptides. The invention also describe molecules which mimic a WW-domain (as required by claim 8) (column 2, lines 8-12). The invention further includes a method for modulating the activity of a ligand or ligand-mimic for a WW-domain, or a WW-domain containing polypeptide, wherein the modulation is inhibition or enhancement (column 2, lines 38-45), as in claims 4-5. Furthermore, test substances can act as antagonists or agonists, as well (claim 3) (column 3, lines 39-40; column 11, lines 9-17). Test substances are added to the WW-domain polypeptide either before or following the addition of the ligand under conditions suitable for maintaining WW-domain and ligand in a conformation appropriate for formation of a combination (column 10,

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lines 61-65). X-ray and NMR structural analysis are used to identify the salient features of the WW-domain (column 18, lines 23-31). In order to determine the structural basis for binding specificity, mutagenesis, and molecular modeling were performed on the Pin1 crystal structure (see Example 6 beginning column 24).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the WW domain structural and functional information provided by Raganathan et al., as was done by Verdiccia et al. (see page 639, column 2, lines 32-39, for example) to contact a WW domain with its substrate or to contact the WW domain with a potential binding agent, whether it be an agonist, antagonist, inhibitory agent etc., as is done by Lu et al. It is well known in the field of crystallography that modeling programs are used to generate three-dimensional representations of molecules along with their binding partners. It would have been obvious to use all of the crystallographic structural and functional information available in the prior art to determine a binding agent of a WW domain.

No claims are allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (703) 306-5439. The examiner can normally be reached on Monday-Friday from 10am to 6:30pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

June 30, 2003

Lori A. Clow, Ph.D.

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Lori A. Clow

MP Woodward
SPC Art 1631